Who Needs What Imaging, and When?
And, Who is Not a Candidate for Surgery?

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Disclosure

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• Earn livelihood (salaried) from caring for children with epilepsy
• Co-Investigator (Not PI & no salary support) on several Pharmaceutical Industry supported AED clinical trials: Rectal Diazepam, Oxcarbazine, Lamotrigine, Zonisimide, Vigabatrin, Tiagabine, Gabapentin, Clobazam, Rufinimide.
• Spouse: Industry trials and consultant (Psychiatry)
• Stock: General Electric and Siemens
• I do use pens and flashlights from industry with logo.
Epilepsy, Imaging, & Surgery

- Confirmation of focus (critical for epilepsy surgery)
- Identify areas to be spared during epilepsy surgery (cortical and white matter)

Gaillard WD et al Epilepsia 2009
Imaging

- Structural high resolution MRI, epilepsy protocol
- PET
- SPECT
- MEG/3D EEG
- fMRI-EEG
- DTI focus localization: Not yet effective
- Connectivity analysis: Not yet stable/reliable
- Functional Mapping Cortex (fMRI, MEG, TMS)
- White Matter Tracts

- There is NO substitute for a high quality epilepsy sequence MRI preferably at 3T (relevant findings in 20-50% of patients with newly diagnosed epilepsy)

MRI Epilepsy Protocol (>2 yrs):
To optimize detection of structural lesions

- High Resolution 3D T1 weighted (SPGR) 1 mm
  - Preferably acquired in sagittal plane (for motion)
- Axial & Coronal T2
- Axial & Coronal FLAIR
- Oblique Coronal High resolution (<4mm) FSE \( \perp \) to the long axis of the hippocampal formation
- Gadolinium contrast not necessary unless tumor or inflammation suspected
Epilepsy: protocol continued

- Standard sequences with increased resolution
  - 3 Tesla MRI units better than 1.5 Tesla (or lower)
  - Decrease slice thickness
    - From 4-5 mm to 1-2 mm
    - Normal cortex is about 2 mm in thickness
    - Thicker images may not reveal focal lesions
- Pulse sequences not used in common practice
  - magnetization transfer, MR spectroscopy, susceptibility imaging, DTI, ASL
- Infants (< 2yr)
  - T2 Axial, coronal, sagittal (or 3D)
  - 3D T1 less useful
MRI Abnormalities: Children New Onset Seizures

Significant findings in 108/390 (28%) studies

ILAE 2004 Pediatric Epilepsy Surgery Survey

- MCD/FCD 42%
- Tumor 20%
- Stroke 10%
- MTS 7%
- Gliosis/No clear pathology 6%
- TS 5%
- Hypothalamic Hamartoma 3%
- Rasmussen 3%
- Vascular (include Sturge Weber) 4%

Harvey AS et al., Epilepsia 2008
Class 1A Seizure Outcome
2004 ILAE Pediatric Outcome Survey

Pre-Surgery MRI + (n=652; 88%)
  Class 1A: 58%

Pre-Surgery MRI – (n=89; 12%)
  Class 1A: 29%

MRI + Complete (62%)
  Class 1A: 83%

“Complete” Resection (58%)
  Class 1A: 44%

MRI + Incomplete (38%)
  Class 1A: 16%

“Incomplete” Resection (42%)
  Class 1A: 3%

*PET/SPECT/MEG+ 40-60% EI; Image - <30%

Courtesy G Mathern
Vascular

Cavernoma  AVM  Stroke
Mesial Temporal Sclerosis
Focal cortical dysplasia

Can be obvious, subtle, or totally normal
Unilateral Lt TE WM hypomyelination
2 y.o., severe (catastrophic) focal right sided seizures, left hemiparesis
Pulse sequences not used in common practice
Magnetization transfer (better at 1.5T than 3T!)

7 y.o., right parietal sz
Structural MRI

- Special sequences/ imaging infants
- Timing imaging dysplasia in infants: They come and go: Best <4mo; > 24mo
- …..and Repeat if normal and seizing q 3-6 mo

7 days   1 year   2 years
• FCD IIIA. Not seen 18 mo, apparent 4 yrs
MRI Negative & Image Negative

- “outside” MRI negative
- “outside” MRI reviewed and negative
- 1.5 T MRI epilepsy protocol negative
- 3T MRI epilepsy protocol negative
- Then perform PET, SPECT, or source localization
- 3T epilepsy protocol reviewed after vEEG, PET, SPECT, &/or source localization (MEG, 3D EEG) = MRI negative

- Image negative: MRI, PET, SPECT, MEG

- If Image Positive good to excellent likelihood of seizure control; if Image negative outcome poor

Imaging: FDG-PET

- Measure of metabolic rate (synapse): Glucose uptake and consumption
- Ictal FDG-PET uncommon and unreliable
- Interictal: Regional hypometabolism lateralizes the seizure focus; less reliable localizing focus
- Regional hypometabolism more widespread than epileptogenic zone
- Regional hypometabolism: Good surgical outcome adults with childhood onset epilepsy (class 2)
- Reduces need for invasive (less extensive) recording
18FDG-PET

- Correctly lateralize focus in 60% children with intractable partial epilepsy (including those with normal MRI)
- May be helpful in young, < 2 years, when MRI less sensitive to identifying dysplasia (Class 4)
- Evaluate integrity good hemisphere when considering hemispherectomy (Class 4)
- Fluctuating findings in children with infantile spasms (Class 4)
Truly sharply demarcated and focal PET
More likely to have clear FCD

$^{11}$C α- Methyl Tryptophan

- Precursor to Serotonin synthesis
- Likely precursor to quinolinic and kynurenic acid – implicated as excitatory compounds
- Increased in epileptogenic Tubers TS
- Increased in focal cortical dysplasia
- Increased in non lesional epilepsy, dysplasia, especially young (sensitivity 50%)
- Increase in surgical margins in surgical failures
AMT-PET Tuberous Sclerosis

Helpful in one third of patients evaluated for epilepsy surgery
95/191 laterialized; AMT-PET in 68/95

n=191  
Chugani HT et al, Neurology 2013
SPECT

- HMPAO, ECD (99-Technetium)
- Markers of CBF
- Long half life (6 hours)
- Can scan several hours after injection
- Can not quantify
- Always perform with EEG
- Timing of injection in relation to seizure critical
SPECT

- Interictal, SuSPECT: False lateralizing 10%
- Ictal Superior
- Subtraction Inter-Ictal from Ictal (or SPM)
  - Co-registration with structural MRI
  - Increases inter and intra rater agreement from 70 to 85% & localization value 31-74% to 74-93%
  - 80-90% when lesion present
  - 59-76% non lesional
- Reliability depends on timing/delay injection in relation to seizure onset (later injection increases false localization/lateralization)
- Propagation effects
  O’Brien et al, 98, 99; Vera et al, 99
Ictal SPECT
Co-registered with MRI

Courtesy G Cascino

Courtesy P Jayakar MCH
interictal
post-ictal

 Courtesy C Chiron
Source Imaging

- 3D EEG
- MEG (w and w/o EEG) not so good radial/deep
- fMRI (EEG triggered)
- 30% patients do not have spikes, insufficient spikes, or technically inadequate
- Helpful in ~60% patients with normal MRI
- Temporal (MEG) and spatial resolution (MRI)
- Utility proportional to relation interictal abnormalities to ictal onset zone
- Multifocal and diffuse: worse/poor outcome
- Single and clustered: better/good outcome
T1

EEG-fMRI

Courtesy JH Cross; GOSH, UCL
MEG & FCD
2nd Look
Tiege et al, Neurosurgery, 2012

Dipole & SAM
N=160; 77 iEEG; 72 Seizures; 62 resection; 38 (61%) Engle I MRI negative (43%), unclear, small FCD

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Motor Mapping

Tongue Wiggling

Hand Tapping

L Foot Tapping
fMRI & IAT (Wada)

Janecek et al, Epilepsia, 2013

32/229 discordant
86% concordant
14% discordant

fMRI > IAT for Predicting outcome
fMRI Language Group Maps for Children Ages 4-12 years (n=68, p<0.05 corrected)

Auditory Category Decision

Listening to Stories

Auditory Description Decision Task

Reading Stories (6-12, n=48)
30% MRI negative patients will have atypical language dominance.

Auditory Description Decision Task

Auditory Category

Listening to Stories

Reading Stories
fMRI Semantic Decision Task Predicts Post-Op Naming

AI > 0.4 risk of language measure decline

Failed fMRI

- Disruption **BOLD** Signal
  - Glioma, Edema & Mass Effect (Bookheimer et al, 1997)
  - AVM and Vascular Steal (Lehericy et al, 2002)
  - Post-Ictal state (Jayakar et al, 2002)
  - Arterial Stenosis (Rother et al, 2002)
DTI Tractography: White Matter, Anatomic, Functional Seed Language, Meyers Loop, Motor Tracks

Multi-Modal Imaging

fMRI Language Comprehension (Listening to stories)

DTI Tractography
Arcuate Fasciculus

FDG-PET

MRI
9 children presented at Epilepsy Conference With normal MRI

Seemingly focal vEEG Seizure (w/ time multifocal)

One focal PET

6 SCN1A
2 SCN2A
(1 CHRNA2)
Genome-wide association study

1,018 people with mTLE & MTS;
7,552 control subjects,

Validation independent sample

959 people with mTLE & MTS;
3,591 control subjects.

Cases with mTLE with MTS
w/ (n = 757) & w/o (n = 803)
febrile seizures

Significant association for
mTLE, MTS, & febrile seizures
w/ SCN1A gene, P:3.36 ×10(-9),
odds ratio (A) = 1.42,
95% confidence interval: 1.26-1.59].

Kasperaviciute D et al., *Brain*, 2013
Cause of epilepsy established (though may search for genes)
Prognosis for seizure control poor
Not candidates for “curative” epilepsy surgery
Metabolic Imaging
Not candidates for “curative” epilepsy surgery
Epilepsy Surgery Evaluation Protocol

ILAE
Summary I

• There is no substitute for a high quality, high resolution, MRI epilepsy protocol (preferably at 3T) reviewed at initial evaluation and after non invasive evaluation (neurophysiological and functional imaging) by skilled readers of pediatric MRI

• Willie Sutton’s rule: It is about the lesion

• Who needs MRI: everyone

• When: preferably at onset, certainly when two medications failed the child
Summary II

- Clear MRI Lesion: PET, SPECT, MEG add little
- FDG-PET: Non-lesional MRI helpful 60% (>TLE)
- SPECT/MEG when PET negative or unavailable
- FDG-PET, iSPECT, MEG about 60-70% helpful
- FDG-PET lateralizes, iSPECT, MEG better localization but more propagation effects
- Use modality with greatest access and skill as comparable, may be complementary, all limitations
- Negative or discordant results, & negative genetic testing then consider invasive monitoring & higher risk of poor outcome
Summary III

- fMRI provides reliable data to identify eloquent cortex, and to guide localization of critical cortical functions: motor, sensory, language, (and memory)
- DTI provides means to identify long and short white matter tracts that convey eloquent function
- Connectivity analysis in infancy and may hold promise for identifying ictal source, networks, and eloquent function
- Outcome related to resection of MRI abnormality, not PET, SPECT, or MEG abnormality